Questioning the Value of Fluorodeoxyglucose Positron Emission Tomography for Residual Lesions After Chemotherapy for Metastatic Seminoma: Results of an International Global Germ Cell Cancer Group Registry

Cathomas, Richard ; Klingbiel, Dirk ; Bernard, Brandon ; Lorch, Anja ; Garcia Del Muro, Xavier ; Morelli, Franco ; De Giorgi, Ugo ; Fedyanin, Mikhail ; Oing, Christoph ; Sagstuen Haugnes, Hege ; Hentrich, Marcus ; Fankhauser, Christian ; Gillessen, Silke ; Beyer, Jörg

Abstract: PURPOSE Residual lesions after chemotherapy are frequent in metastatic seminoma. Watchful waiting is recommended for lesions < 3 cm as well as for fluorodeoxyglucose (FDG) positron emission tomography (PET)-negative lesions 3 cm. Information on the optimal management of PET-positive residual lesions 3 cm is lacking. PATIENTS AND METHODS We retrospectively identified 90 patients with metastatic seminoma with PET-positive residual lesions after chemotherapy. Patients with elevated -fetoprotein or nonseminomatous histology were excluded. We analyzed the post-PET management and its impact on relapse and survival and calculated the positive predictive value (PPV) for PET. RESULTS Median follow-up time was 29 months (interquartile range [IQR], 10 to 62 months). Median diameter of the largest residual mass was 4.9 cm (range, 1.1 to 14 cm), with masses located in the retroperitoneum (77%), pelvis (16%), mediastinum (17%), and/or lung (3%). Median time from the last day of chemotherapy to PET was 6.9 weeks (IQR, 4.4 to 9.9 weeks). Post-PET management included repeated imaging in 51 patients (57%), resection in 26 patients (29%), biopsy in nine patients (10%) and radiotherapy in four patients (4%). Histology of the resected specimen was necrosis in 21 patients (81%) and vital seminoma in five patients (19%). No biopsy revealed vital seminoma. Relapse or progression occurred in 15 patients (17%) after a median of 3.7 months (IQR, 2.5 to 4.9 months) and was found in 11 (22%) of 51 patients on repeated imaging, in two (8%) of 26 patients after resection, and in two (22%) of nine patients after biopsy. All but one patient who experienced relapse were successfully treated with salvage therapy. The PPV for FDG-PET was 23%. CONCLUSION FDG-PET has a low PPV for vital tumor in residual lesions after chemotherapy in patients with metastatic seminoma. This cautions against clinical decisions based on PET positivity alone.

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Questioning the value of FDG PET for residual lesions after chemotherapy for metastatic seminoma: results of an International Global Germ Cell Cancer Group registry

Richard Cathomas[1], Dirk Klingbiel[2], Brandon Bernard[3], Anja Lorch[4], Xavier Garcia del Muro[5], Franco Morelli[6], Ugo De Giorgi[7], Mikhail Fedyanin[8], Christoph Oing[9], Hege Sagstuen Haugnes[10], Marcus Hentrich[11], Christian Fankhauser[12], Silke Gillessen[13], Jörg Beyer[14]

Affiliations:
[1]Division of Oncology/Hematology, Kantonsspital Graubünden, Chur, Switzerland
[2]SAKK Coordinating Center Bern, Switzerland
[3]Dana-Farber Cancer Institute Boston, USA
[4]Department of Urology, University of Düsseldorf, Germany
[5] Institute Catalan of Oncology. IDIBELL. University of Barcelona for the Spanish Germ cell Cancer Group
[6]Department of Oncology, San Giovanni Rotondo, Italy
[7]IRST IRCCS, Meldola, Italy; for the Italian Germ cell cancer Group
[8]Department of clinical pharmacology and chemotherapy N.N. Blokhin National Medical Research Center of Oncology Moscow, Russia
[9]Department of Oncology, Hematology and Bone Marrow Transplantation with Section of Pneumology, University Medical Center Hamburg-Eppendorf, Germany
[10]Department of Oncology. University Hospital of North Norway, and UIT-The Arctic University, Tromso, Norway
[11]Department of Oncology, Rotkreuzklinikum München, Germany
[12]Department of Urology, University of Zürich, Switzerland
[13]Department of Oncology, Kantonsspital St.Gallen, and University of Bern, Switzerland
[14]Department of Medical Oncology, Inselspital, Bern University Hospital, University of Bern, Switzerland

Corresponding author:
Richard Cathomas, MD
Division of Oncology/Hematology
Kantonsspital Graubünden
CH-7000 Chur
Switzerland
Tel: +41 81 256 6646
Fax: +41 81 256 6668
Email: richard.cathomas@ksgr.ch

Running head: value of PET for metastatic seminoma with residual lesions

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Abstract

Purpose

Residual lesions after chemotherapy are frequent in metastatic seminoma. Watchful waiting is recommended for lesions <3 cm as well as for fluoro-deoxyglucose (FDG) positron-emission tomography (PET) negative lesions ≥3 cm. Information on the optimal management of PET positive residual lesions ≥3 cm is lacking.

Patients and Methods

We retrospectively identified 90 metastatic seminoma patients with PET positive residual lesions after chemotherapy. Patients with elevated AFP or non-seminomatous histology were excluded. We analyzed the post PET management, its impact on relapse and survival and calculated the positive predictive value (PPV) for PET.

Results

Median follow-up was 29 months (interquartile range, IQR 10 – 62). Median diameter of the largest residual mass was 4.9 cm (range 1.1 – 14) located in the retroperitoneum (77%), pelvis (16%), mediastinum (17%) and/or lung (3%). Median time from the last day of chemotherapy to PET was 6.9 weeks (IQR 4.4 – 9.9 weeks). Post PET management was repeated imaging in 51 (57%), resection in 26 (29%), biopsy in 9 (10%) and radiotherapy in 4 (4%) patients. Histology of the resected specimen was necrosis in 21 (81%) and vital seminoma in 5 patients (19%). No biopsy revealed vital seminoma. Relapse or progression occurred in 15 patients (17%) after a median of 3.7 months (IQR 2.5 – 4.9 months): in 11/51 (22%) patients on repeated imaging, in 2/26 (8%) patients after resection and in 2/9 (22%) patients after biopsy. All but one relapsed patients were successfully salvaged. PPV for PET was 23%.

Conclusion

FDG-PET has a low PPV for vital tumor in residual lesions post chemotherapy in patients with metastatic seminoma. This cautions against clinical decisions based on PET positivity alone.

Keywords:

FDG PET, residual lesion, metastatic seminoma, positive predictive value

Introduction

More than 50% of all germ-cell tumors are seminomas and the majority present with localized stage I disease at diagnosis. However, 20-30% of seminoma patients will develop metastatic disease (1, 2) and be successfully treated with 3 - 4 cycles of cisplatin-based combination chemotherapy (3, 4). Residual masses after chemotherapy are frequent and can be found in up to 80% of men with advanced stage (5 - 7). There is an ongoing controversy regarding the optimal post-chemotherapy management of residual masses more than 3 cm in diameter. In contrast to non-seminomatous germ cell tumors ("non-seminomas"), post chemotherapy residual masses in seminomas almost exclusively contain necrosis, especially if they are smaller than 3 cm. PET scans are not recommended for these patients. In patients with residual masses of 3 cm or larger, viable cancer is occasionally found (7 – 9) and may be identified by [^{18}F]-fluoro-deoxy-D-glucose (FDG) positron emission tomography (PET) scanning. The first prospective study investigating the use of PET in this situation demonstrated a negative predictive value of up to 96%, and a positive predictive value (PPV) of 100%, but subsequent studies showed that the PPV was only 42% (10, 11).

Currently, there is no undisputed strategy regarding how to manage seminoma patients with PET positive lesions post chemotherapy. Therefore, we decided to perform a retrospective data collection in order to analyze treatment patterns and outcomes of such patients.

Patients and Methods

Centers collaborating within the Global Germ-Cell Cancer Group were contacted to share data of patients with metastatic seminoma and PET-positive residual lesions post chemotherapy. Detailed information was collected anonymously using structured questionnaires, and the planned data analysis was predefined in a priori written protocol (supplement 1). Approval of the local ethical committees was obtained before data collection.

The following items were included: patient characteristics at the time of starting chemotherapy for metastatic disease; chemotherapy regimen as well as any additional treatment modalities and the best response to it; time from last day of chemotherapy to first PET; detailed PET results as determined by the local investigator including standard uptake value (SUV) and visual interpretation of equivocal vs definite positivity; post-PET management decisions (repeated imaging vs resection vs biopsy vs radiotherapy); outcome according to the post-PET management decisions (relapse, histology of resected specimen or biopsy); treatment of relapse and outcome. Relapse was defined as significant rise of HCG tumor marker or unequivocal progression in size of residual lesions or appearance of new lesions. Data were anonymized locally, transferred and entered into a joined database hosted by the Swiss Working Group for Clinical Cancer Research (SAKK) in Bern, Switzerland.

Patients

The following inclusion criteria were applied: male sex, age 18 years or older, histologically confirmed pure seminoma, serum AFP < 2x ULN at any time; curative intent chemotherapy for stage IIB, IIC or III; residual masses with increased FDG uptake on PET imaging (according to local investigator) after completion of chemotherapy.

Patients were excluded, if they had non-seminomatous histology or any other histology apart from seminoma, progressive disease at the time of first PET assessment (rising HCG or unequivocal progression on imaging), or if they had other malignant diseases. Patients with responses (partial response with ≥30% size reduction, HCG negative), or with stable disease (tumor reduction <30%, no growth ≥20%, HCG negative) as best response post-chemotherapy were eligible. Patients with a response, but persistently elevated LDH were classified as marker-positive partial remissions (PRm+). Disease stage was reported according to the International Union against Cancer classification

(12). For allocation into risk categories, the prognostic classification of the International Germ Cell Cancer Consensus Group (IGCCCG) was used (13).

Statistical analysis

The primary objectives were the management and outcomes (relapse or histological finding of vital seminoma) of patients with a positive PET scan and the association between outcome and potential prognostic factors. Secondary objectives were the time from the end of chemotherapy to the first PET, the histologies of resection specimens and biopsies, the treatments and outcomes of relapses and the calculation of the PPV of PET.

Follow-up was calculated from the day of the first PET to the date of last contact. Positive PET scans were rated as true positive, if either viable tumor was detected histologically or relapse was diagnosed clinically during follow-up as defined by significantly increasing HCG tumor marker or unequivocal progression on imaging; all other positive PET scans were rated false positive. Continuous data were summarized using median and range, categorical data using frequency counts and percentages, and time-to-event endpoints via the Kaplan-Meier method using median and interquartile range (IQR). Fisher's exact test was used to check univariate associations between variables.

Results

Data from 95 patients with metastatic seminoma and PET-positive post-chemotherapy residual masses detected between March 2003 and September 2016 in 18 different centers/groups from 9 different countries were identified. Five patients were excluded due to ineligibility, including PET negativity in three patients and clinically progressive disease at date of first PET in two patients. Therefore, 90 patients with a median follow up of 29 months (IQR 10 – 62 months) were considered eligible according to protocol and included in the analysis (Figure 1).

Patient characteristics

Detailed patient characteristics are shown in Table 1. The median size of the largest PET positive residual mass was 4.9 cm (range 1.1 – 14 cm). Only 8 patients (9%) had a residual mass of less than 3 cm. The clinical setting before PET was first line treatment in 87/90 (97%) patients including 80 patients with primary metastatic disease, 3 relapses after adjuvant carboplatin, 2 patients with relapses on active surveillance, and one patient each with disease progression after adjuvant radiotherapy or radiotherapy for stage IIB disease, respectively. In 3 patients (3%) the clinical setting was salvage treatment after prior chemotherapy of metastatic disease (one patient each for stage IIB, IIC, III, respectively). Chemotherapy consisted of standard bleomycin, etoposide and cisplatin (BEP) x 3 in 44 patients (49%), more intensive treatment with BEP x 4 in 21 patients (23%), BEP x3 plus 1x etoposide and cisplatin (EP) in 5 patients (6%), standard EP x 4 in 8 patients (9%); and other miscellaneous platinum-based combination regimens in 12 patients (13%).

Primary management and outcome

The management of PET-positive patients is shown in Figure 1. The majority of 51/90 (57%) patients were followed with repeated imaging (including PET, CT or ultrasound), and 11/51 (22%) of them experienced a relapse. In 26/90 (29%) patients the management consisted of surgical resection, of whom 2/26 (8%) patients had a relapse. 9/90 (10%) patients had a biopsy and 2/9 (22%) of them relapsed. Radiotherapy was performed in 4/90 (4%) patients, in whom no relapses occurred.

Repeated imaging

Among the 51 patients with repeated imaging, overall 39/51 (76%) had a subsequent PET. The median time to next PET scan was 2.9 months. In 6/39 (15%) patients the PET became negative and no relapses occurred in those six patients. Overall 33/39 (85%) had a positive PET scan on repeated imaging. Resections were performed in 6/33 (18%) of these patients, among whom two had seminoma in the resected specimens and no further relapses were observed. The remaining 27/33 (82%) patients were followed with repeated imaging and 7/27 (26%) relapses occurred. Therefore, even in case of repeated positive PET scans no relapse or vital seminoma was found in 24/33 (73%) patients. Another 12/51 (24%) patients had CT, of whom 4/12 (33%) progressed.

Surgical Resection

In total 32/90 (36%) patients underwent resection of a PET positive residual lesion: 26/32 (81%) as immediate resections after the first positive PET, and 6/32 (19%) patients after a subsequent PET which demonstrated continued positivity. The majority of resections were performed in 29/32 (91%) patients on masses in the retroperitoneum and/or pelvis, and only three resections in the mediastinum. Vital seminoma was found in 5/26 (19%) patients with immediate resection of PET positive lesions, and in 2/6 (33%) of patients with a second positive PET scan. In the remaining 25/32 (78%) of patients only necrosis was found. One of the resected patients received 2 cycles of adjuvant cisplatin/etoposide chemotherapy, and two were treated with postoperative adjuvant radiotherapy to the resection site. Viable seminoma was found in the retroperitoneum or pelvis, but not in the mediastinum. Two patients suffered a relapse at the resection site after immediate surgery of PET positive lesions despite reported complete resections: one after resection of necrosis, and one after resection of vital seminoma. Local investigators reported serious postoperative complications in 6/32 (19%) patients including chylous ascites, pulmonary embolism, bilateral jugular deep vein thrombosis, retroperitoneal hematoma, adhesion with intestinal pseudo-obstruction and retrograde ejaculation.

Biopsy

Biopsies for histological assessment were obtained using core needle biopsies or open techniques (e.g. mediastinoscopy). None of the nine biopsies from PET positive residual masses revealed seminoma on histological workup. The following histological results

were found: sarcoidosis (n=2), necrosis (n=2), fibrosis (n=1), abscess (n=1), reactive lymphoid tissue (n=1), desmoid tumor (n=1) and schwannoma (n=1). Two relapses occurred at biopsy sites: One relapse was identified after 67 days in a patient in whom the initial post chemotherapy biopsy had shown necrosis. The other relapse occurred in a PET-negative retroperitoneal residual mass 28 days after a biopsy had shown schwannoma at a PET-positive pre-sacral lesion.

Radiotherapy

Only 4 patients had immediate radiotherapy of a residual PET positive lesion without further diagnostic procedures. One patient had received high-dose chemotherapy and autologous stem cell transplant for relapsed seminoma and demonstrated a PET positive residual lesion in the right iliac/inguinal area. The other three patients had retroperitoneal disease after BEP: two patients with marker-negative PET-positive partial remissions, and one patient with marker-negative PET-positive stable disease. None of the irradiated patients experienced a relapse.

Risk factors for relapse or presence of vital seminoma and outcome of relapse

The risk of relapse or presence of vital seminoma in the resection specimen according to different clinical variables was investigated in univariate analyses (Supplement Table 1): no factor achieved statistical significance. Visual interpretation of FDG activity and response to prior chemotherapy revealed a trend (p=0.06). To further elucidate the impact of visual PET interpretation, we analyzed the relapse rate for each primary management according to visual PET interpretation demonstrating no major imbalance between the groups (Supplement Table 2). Actual SUV results were available for 73/90 patients (81%): patients with relapse had higher SUV values (median SUV 4.2 vs 3.6; p=0.02), but no cut-off with an improved positive predictive value could be defined.

Table 2 presents a summary of all 15 relapsed patients. Relapses occurred within a maximum of 129 days after initial PET or resection/biopsy, respectively. Two out of five patients with PRm+ and four out of eight patients with stable disease experienced a relapse or had vital seminoma in the resected specimen. Of note, relapses occurred at the site of residual masses in all patients, in three patients additional metastatic sites were found. One patient died during salvage treatment from progressive disease, but all other patients could be successfully salvaged using conventional-dose chemotherapy in

two patients, and high-dose chemotherapy followed by autologous stem cell transplant in 12/15 (80%) patients.
At the time of last follow up, 56/90 (62%) patients were reported to be in complete remission, 32/90 (36%) patients had residual, but inactive disease, one patient was lost to follow up and one patient had died from progressive disease.

Positive predictive value of PET

The PPV of PET was calculated for all patients as well as for the following subgroups: equivocal or definite PET positivity on visual interpretation; PET performed within 6 weeks after last day of chemotherapy or later; SUV cut-off of 4; size of residual lesion cut-off 3cm. The results are shown in table 3. The PPV for the entire patient population is low at 23%. None of the subgroups revealed meaningful improvement of PPV with values of 29% for patients with definite PET positivity, 19% if PET was performed later than 6 weeks after the end of chemotherapy, 32% in case of SUV 4 or higher and 22% if the residual lesion was 3 cm or larger.

Discussion

This report summarizes the results of the analysis of the largest cohort of metastatic seminoma patients with PET positive residual masses after chemotherapy. In contrast to previous smaller series with only few PET-positive patients included (ranging from 8 to 33 patients), our data could not confirm a favorable PPV of PET in this setting (10, 11, 14, 15). We calculated a PPV of only 23% for a group of patients that consisted mainly of the target population with residual masses larger than 3 cm. Subgroup analyses using more stringent additional criteria including unequivocal PET positivity, elevated SUV of 4 or more, PET scanning later than 6 weeks after the end of chemotherapy and residual mass size of 3cm or larger, did not substantially improve the PPV: it resulted in PPV of only 29%, 32%, 19% and 22%, respectively.
The reason for the high rate of false-positive PET can be explained by the histological findings: Among 41 patients with further evaluation of positive scans by either biopsy or resection, vital seminoma was only found in 7/41 (17%). Necrosis was the most

frequent finding, but other histologies such as sarcoidosis, fibrosis, inflammation and benign tumors were also associated with false positive FDG activity.

Relapses were detected in 17% of patients, all at the site of residual disease and all within 4 months after the end of chemotherapy. Importantly, all but one relapses could successfully be salvaged by conventional-dose or high-dose chemotherapy. This suggests that intensified or prolonged follow up of PET-positive seminoma patients or repeated PET scanning is unnecessary, because patients with residual vital seminoma will eventually be identified by regular follow-up schedules.

Patients undergoing surgical resections of PET-positive residual masses had a low relapse rate of only 8% as compared to 22% in case of follow-up using repeated imaging. This corresponds to an absolute risk reduction of 14% and a relative risk reduction of 64%. Based on these figures, the "number-needed-to-resect" in order to prevent one relapse would be eight. Resections of large post-chemotherapy masses in seminoma are challenging, however, and often associated with severe complications (16). Moreover, the fact that necrosis was the only histological finding in about 80% of resected patients confirms that PET is an inappropriate tool to reliably predict viable seminoma after chemotherapy, or to identify patients who might benefit from additional post-chemotherapy treatments. In the near future, novel serum biomarkers such as microRNA might help to identify patients with vital residual tumor (17).

None of four PET-positive patients relapsed after additional radiotherapy. However, as no histological information is available in those patients, the impact of additional radiotherapy cannot be assessed. The use of additional radiotherapy is nevertheless discouraged in patients with PET-positive residual lesions since the likelihood of overtreatment is high (18, 19) and late toxicities after treatment with both chemotherapy and radiotherapy are known to be markedly increased (20, 21).

An unexpected finding of our analysis is the fact that patients who presented initially with large seminoma masses may have been exposed to overtreatment: while only 9% of patients were classified as intermediate risk according to the IGCCCG classification, a total of 29% of patients received four cycles of a cisplatin-based three drug combination. Hence, one of five patients may have received a forth cycle possibly on the impression of large tumor masses and/or elevated LDH, which is not recommended by current guidelines.

This report has all the limitations inherent in a retrospective study and is only hypothesis generating. The data are susceptible to selection bias and may not be representative for all seminoma patients; e.g. among 8 patients with residual lesions < 3 cm the rate of viable seminoma/relapse was unexpectedly high. Moreover, as we did not centrally reassess the original PET scans, we had to rely on assessments by local investigators, which might have introduced inter-observer bias. The fact that technical improvements in PET scanning and reporting had occurred during the study period, and that current "state-of-the-art" SUV measurements are not available for all patients in this series is another drawback.

While our report represents the largest analysis in this patient population, the total number of patients is still small. Without prospective randomized studies, no definite recommendations as to the optimal management of seminoma patients with residual masses post-chemotherapy can be made. As the probability of vital seminoma is reported to be low in most series, there is consensus amongst experts that PET should not be used in residual lesions measuring less than 3cm in the largest diameter (3). Such patients can be followed according to published guidelines (3, 4), with imaging (MRI or CT) after 6 and 12 months and annually thereafter up to five years. For residual lesions 3cm or larger, we recommend to perform PET not earlier than 6 weeks after completion of chemotherapy. In view of the high negative predictive value of 96% (11), PET negative patients can be followed according to the aforementioned schedule. In case of a positive PET post-chemotherapy, we propose to closely monitor patients with repeated imaging (CT or MRI), tumor marker measurements and clinical assessment after 2 and 4 months and every four months thereafter in the first year, every six months in the second year and then annually up to five years. Based on the results of the current analysis, biopsies of residual lesions are discouraged. Surgical resection of PET positive residual lesions may be considered on an individual basis based on size, location, resectability and patient preference. For patients with unequivocal progression salvage chemotherapy is recommended and will result in a high rate of cure.

Despite its limitations, the results of this retrospective study challenge the clinical relevance of positive PET scans in patients with metastatic seminoma and residual masses after chemotherapy and caution against additional treatments based on PET-positivity alone. Given their rarity and complexity, such patients should be referred to centers with expertise in managing germ cell tumors.

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The following individuals have also contributed patient data:

Gaetano Aurilio, Department of Medical Oncology, IEO, Milano, Italy
Umberto Basso, Department of Medical Oncology, IOV IRCCS, Padova, Italy
Margarida Brito, Medical Oncology Department Instituto Português de Oncologia de Lisboa, Portugal;
Gabriella Cohn-Cedermark, Department of Oncology-Pathology, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden;
Gedske Daugaard, Department of Oncology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark;
Giuseppe Fornarini, Department of Medical Oncology, IRCCS AOU San Martino-IST, Genova, Italy;
Francesca Maines, Department of Medical Oncology, Santa Chiara Hospital, Trento, Italy
Frank Mayer, Department of Medical Oncolgy, University Tübingen, Germany;
Daniel Maria Meyer, Department of Hemato-Oncology, Landeskrankenhaus Hochsteiermark, Leoben, Austria

Figure legend and Tables:

Figure 1. Overview of patients
*one patient with seminoma in the resected specimen had a later relapse and is included in both boxes

Table 1. Patient characteristics

	All Patients N=90	Follow up N=51	Resection N=26
Median age (range)	41 years (19 – 69)	40 years (19 – 69)	43 years (25 – 53)
Primary tumor			
gonadal	67 (75%)	36 (71%)	20 (77%)
retroperitoneal	10 (11%)	8 (16%)	5 (19%)
mediastinal	12 (13%)	7 (14%)	1 (4%)
IGCCCG risk group			
Good	80 (91%)	46 (94%)	23 (88%)
Intermediate	8 (9%)	3 (6%)	3 (12%)
Elevated LDH at diagnosis	64 (71%)	37 (73%)	21 (81%)
Elevated HCG at diagnosis	54 (60%)	33 (65%)	14 (54%)
Largest residual mass, median (range)	4.9 cm (1.1 – 14)	4.6 cm (1.1 – 13.1)	5.0 cm (2.3 – 14)
Site of Residual mass			
Retroperitoneum	69 (77%)	36 (71%)	24 (92%)
Pelvis	14 (16%)	6 (12%)	7 (27%)
Mediastinum	15 (17%)	11 (22%)	1 (4%)
Lung	3 (3%)	2 (4%)	0
Time from last day of chemo to first PET (IQR)	6.9 weeks (4.4 – 9.9)	7.3 weeks (5.0 – 10.6)	6.0 weeks (3.9 – 8.4)

Abbreviations: IGCCCG, International Germ Cell Cancer Collaborative Group; IQR, interquartile range

Table 2. Overview of all relapsed patients

UPN	Immediate post-chemo management	Overall best response to first line treatment	Size + localization of residual disease	SUV max.	Time to relapse (weeks)	Method Diagnosis of relapse	Localisation of relapse	Management Outcome	FU since end salvage (months)
775	**Resection (necrosis)**	SD	14cm, retroperit	2.9	17, post resection	CT	retroperit + new distant	TIP + HDCT CR	74
825	**Resection (<10% vital)**	PRm+ (LDH)	4.2cm, retroperit + pelvis	4.8	8, post resection	CT	retroperit +pelvis	TIP CR	4
742	**Biopsy (necrosis)**	PRm-	11cm, retroperit	7.0	10, post biopsy	HCG rise	retroperit + new lung	HDCT x3 Death on PD	n.a.
773	**Biopsy (schwannoma)**	SD	4.8cm, retroperit	4.1	4, post biopsy	HCG rise	retroperit	1xPEI + 3xHDCT CR	56
730	**FU imaging**	PRm-	10.7cm, retroperit	3.8	18, post 1st PET	PET	retroperit	4xTIP CR	53
737	**FU imaging**	PRm-	6cm, retroperit	n.a.	8, post 1st PET	PET	retroperit	1xTI 3xHDCT resection: necrosis CR	34
745	**FU imaging**	PRm-	2.2cm, pelvis	n.a.	9, post 1st PET	CT	pelvis	3xHDCT + RT CR	12
772	**FU imaging**	PRm-	3.5cm, Retroperit + lung + mediastinum	4.2	13, post 1st PET	PET	Retroperit + Lung + Mediastinum	1xPEI + 3x HDCT resection:necrosis CR	17
800	**FU imaging**	PRm-	7cm, retroperit	8.4	3, post 1st PET	CT	Retroperit	3x PEI residual inactive	35
803	**FU imaging**	PRm-	4.5cm, retroperit	3.4	14, post 1st PET	PET	Retroperit	TI-CE HDCT residual inactive	33
804	**FU imaging**	PRm-	3cm, retroperit + pelvis + lung	9.2	5, post 1st PET	PET	Lung	TI-CE HDCT residual but inactive	25
805	**FU imaging**	PRm-	3.5cm, pelvis	3.3	17, post 1st PET	PET	Pelvis	TI-CE HDCT: CR	31
806	**FU imaging**	PRm-	12cm, retroperit	9.0	7, post 1st PET	CT	Retroperit	TI-CE HDCT residual inactive	21
807	**FU imaging**	PRm+ (LDH)	3.2 cm,mediastinal, supraclavicular	7.0	5, post 1st PET	CT	Mediastinum + supraclavicular	TI-CE HDCT resection:necrosis CR	10
826	**FU imaging**	PRm-	2.2cm, retroperit	4.0	12, post 1st PET	PET	Retroperit + new bone	TI-CE HDCT RT	54

								CR	

Abbreviations: chemo, chemotherapy; CR, complete remisison; FU, follow-up; n.a., not applicable; PD, progressive disease; PEI, cisplatin/etoposide/ifosfamide; PRm-, partial remission marker negative; PRm+, partial remission marker positive (LDH); retroperit, retroperitoneal; RT, radiotherapy; SD, stable disease; SUV, standard uptake value; TIP, paclitaxel/ifosfamide/cisplatin; TI-CE HDCT, paclitaxel/ifosfamide-carboplatin/etoposide

Table 3. Positive predictive value for all patients and for predefined subgroups

	Viable tumor detected by		True positive N(%)	False positive N(%)	PPV
	Histo	**F/U**			
All pts N=90	7	14	21 (23%)	69 (77%)	23%
PET equivocal, N= 28	2	1	3 (11%)	25 (89%)	11%
PET definite, N= 62	5	13	18 (29%)	44 (71%)	29%
PET ≤6 wks, N=37	4	7	11 (29%)	26 (71%)	29%
PET >6 wks, N=53	3	7	10 (19%)	43 (81%)	19%
PET SUV ≥4, N= 34	3	8	11 (32%)	23 (68%)	32%
PET SUV < 4, N=39	4	4	8 (21%)	31 (79%)	21%
Lesion < 3cm, N=8	1	2	3 (38%)	5 (62%)	38%
Lesion ≥ 3 cm, N= 82	6	12	18 (22%)	64 (78%)	22%

Abbrevations: F/U, follow-up; histo, histology; pts, patients; SUV, standard uptake value; wks, weeks